INTERNATIONAL SEARCH REPORT

International application No
PCT/US04/26344

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/68; AOIN 43/04; C07H 21/04; A61K 31/07
US CL : 435/6, 91.1, 325, 375; 514/44, 536/23.1, 24.33, 24.5
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6, 91.1, 325, 375; 514/44; 536/23.1, 24.33, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JEN et al. Suppression of gene expression by targeted disruption of messenger RNA: Available options and current strategies. Stem Cells. 2000, Vol. 18, pages 307-319, see entire document.	1-31 and 61-67
A	BRANCH , AD. A good antisense molecule is hard to find. TIBS. 1998, Vol. 23, pages 45-50, see entire document.	1-31 and 61-67
A	GREEN et al. Antisense oligonucleotides: An evolving technology for the modulation of gene expression in human disease. J. Am Coll Surg. 2000, Vol. 191, pages 93-105, see entire document.	1-31 and 61-67
A	RICHARDS, IM. Mouse models of allergic disease; how do they relate to asthma in man? Clinical and Experimental Allergy. 1996, Vol. 26, pages 618-620, see entire article.	1-31 and 61-67
A	TEMELKOVSKI et al. An improved murine model of asthma:selective airway inflammation, epithelial lesions and increased methacholine responsiveness following chronic exposure to aerosolised. Thorax. 1998, Vol. 53, pages 849-856, see entire article.	1-31 and 61-67

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents

"A" document deflmngthe general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority clair(s) or which is cited to establish the publication date of another citation or otiier special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document pubhshed prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled m the art

"&" document member of the same patent family

Date of the actual completion of the international search
26 September 2005 (26.09.20051

Date of mailing of the international ! Ï 18V 2005

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Form PCT/ISA/210 (second sheet) (April 2005)

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AOSHIBA et al. Role of p38-Mitogen-Activated Protein Kinase in spontaneous apoptosis of human neutrophils. Journal of Immunology. 1999, Vol. 162, pages 1692-1700, see page 1693, first column, phosphorothioate-modified antisense oligonucleotide.	32-60
Y	HAN et al. A Map Kinase targeted by endotoxin and hyperosmolarity in mammalian cells. Science. 1994, Vol. 265, pages 808-811, see Figure 1.	32-60
Y	AGRAWAL et al. Antisense therapeutics: is it as simple as complementary base recognition? Molecular Medicine Today. 2000, Vol. 6, pages 72-81, see first full paragraph.	32-60
Y	US 5,801,154 A (BARACCHINI et al) 01 September 1998(09.01.1998), see column 7, lines 6-22; column 8, line 12; column 6, lines 12-17; and column 4, lines 26-30.	32-60

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Box No. π Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. HI Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-67, SEQ IDNO:128

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

D No protest accompanied the payment of additional search fees.

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BOX πi. OBSERVATIONS WHERE UNITY OF INVENTION IS LACIONG

Groups 1-252, drawn to an antisense compound targeted to a nucleic acid molecule encoding p38 alpha MAP protein kinase, wherein said compound comprises at least an 8-nucleobase portion of SEQ ID NOs: 90, 128-164, 175-251 , 257-259, 264, 265, 277-314, 316-339, 341 , 343-390, 392, 393-412, and methods of using said antisense compound to inhibit expression of p38 alpha MAP protein kinase in cells or tissues.

The inventions listed as Groups 1-252 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Claims 1-67 are subject to an additional restriction since it is not considered to be a proper genus/Markush. If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claims 1-67 specifically claims antisense SEQ ID NOs. 90, 128-164, 175-251, 257-259, 264, 265, 277-314, 316-339, 341 , 343-390, 392, 393-412, which are targeted to and modulate the expression of p38 alpha MAP protein kinase. Although the antisense sequences claimed each target and modulate expression of p38 alpha MAP protein kinase, the instant antisense sequences are considered to be unrelated, since each antisense sequence claimed is structurally and functionally independent and distinct for the following reasons: each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of p38 alpha MAP protein kinase nucleic acid, and each antisense, upon binding to a p38 alpha MAP protein kinase nucleic acid, functionally modulates (increases or decreases) the expression of the gene and to varying degree (per applicants' Table 1 in the specification). As such, the Markush/genus of antisense sequences in claims 1-39 is not considered to constitute a proper genus, and is therefore subject to restriction. Furthermore, a search of more than one (1) of the antisense sequences claimed in claims 1-39 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed antisense sequences. In view of the foregoing, one (1) antisense sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect one (1) antisense sequence from claims 1-39. Note that this is not a species election.

Thus, in summary, each of Groups 1-252 is directed to different special technical features and thus supports this lack of unity.

Applicants will obtain a search of the first invention listed in the first group. For every other invention applicants wish to have searched, applicants need to elect the group and pay an additional fee. Additionally, applicants will obtain a search of the first sequence listed in the first invention. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

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Continuation of B. FIELDS SEARCHED Item 3:
WEST, STN, Medline, NPL
search terms: p38 alpha, CSaids binding protein, csbp, p38 map kinase alpha, p38 mitogen activated protein kinase, p38 MAPK, antisense, and ribozyme